ACAN gene

aggrecan

Normal Function

The *ACAN* gene provides instructions for making the aggrecan protein. Aggrecan is a type of protein known as a proteoglycan, which means it has several sugar molecules attached to it. It is the most abundant proteoglycan in cartilage, a tough, flexible tissue that makes up much of the skeleton during early development. Most cartilage is later converted to bone (a process called ossification), except for the cartilage that continues to cover and protect the ends of bones and is present in the nose, airways, and external ears.

Aggrecan attaches to the other components of cartilage, organizing the network of molecules that gives cartilage its strength. These interactions occur at a specific region of the aggrecan protein called the C-type lectin domain (CLD). Because of the attached sugars, aggrecan attracts water molecules and gives cartilage its gel-like structure. This feature enables the cartilage to resist compression, protecting bones and joints. Although its role is unclear, aggrecan affects bone development.

Health Conditions Related to Genetic Changes

familial osteochondritis dissecans

At least one mutation in the *ACAN* gene has been found to cause familial osteochondritis dissecans. This condition is characterized by areas of bone damage (lesions) caused by the detachment of cartilage and some of the underlying bone from the end of the bone at a joint. People with familial osteochondritis dissecans have multiple lesions that affect the knees, elbows, hips, or ankles. Other common features are short stature and early development of a painful joint disorder called osteoarthritis.

The *ACAN* gene mutation associated with this condition changes a single protein building block (amino acid) in the CLD of the aggrecan protein. Specifically, the amino acid valine is replaced by the amino acid methionine at protein position 2303 (written as Val2303Met or V2303M). The abnormal aggrecan protein is unable to attach to other components of cartilage. As a result, the cartilage is disorganized and weak. It is unclear how the abnormal cartilage is involved in the development of the lesions and osteoarthritis characteristic of familial osteochondritis dissecans. Researchers have suggested that a disorganized cartilage network in growing bones impairs their growth, leading to short stature.

intervertebral disc disease

other disorders

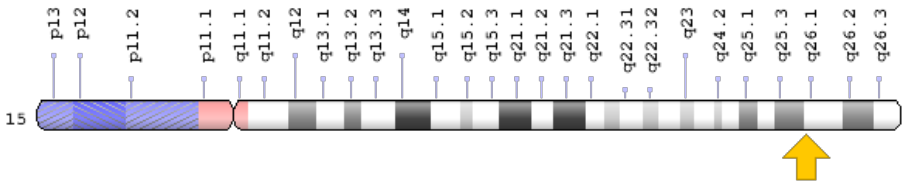
Two other conditions associated with short stature, called spondyloepimetaphyseal dysplasia, aggrecan type and spondyloepiphyseal dysplasia, Kimberley type, are caused by mutations in the *ACAN* gene. People with spondyloepimetaphyseal dysplasia, aggrecan type have extremely short stature, short fingers and toes, and distinctive facial features. This condition is caused by a mutation that changes the amino acid at position 2267 in the aggrecan protein from aspartic acid to asparagine (written as Asp2267Asn or D2267N). The amino acid change, which occurs in the CLD, alters aggrecan's interaction with at least one component of the cartilage network. It is unclear how this change leads to the particular signs and symptoms of spondyloepimetaphyseal dysplasia, aggrecan type.

Spondyloepiphyseal dysplasia, Kimberley type is characterized by short stature and early development of osteoarthritis, particularly in the knees, ankles, and hips. This condition is caused by a mutation in which a single DNA building block is inserted into the *ACAN* gene, which could disrupt the gene's instructions and lead to the production of an abnormally short aggrecan protein that is missing the CLD. It is unknown if the abnormal protein is produced or what effects it might have. It is unclear what role this gene mutation plays in the development of the specific features of spondyloepiphyseal dysplasia, Kimberley type.

Chromosomal Location

Cytogenetic Location: 15q26.1, which is the long (q) arm of chromosome 15 at position 26.1

Molecular Location: base pairs 88,803,442 to 88,875,354 on chromosome 15 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- AGC1
- AGCAN

- aggrecan core protein
- cartilage-specific proteoglycan core protein
- chondroitin sulfate proteoglycan core protein 1
- CSPG1
- CSPGCP
- large aggregating proteoglycan
- MSK16
- SEDK

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth Edition, 2002): Noncollagen Components of the Extracellular Matrix
  https://www.ncbi.nlm.nih.gov/books/NBK21706/

Genetic Testing Registry

- GTR: Genetic tests for ACAN
  https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=176%5Bgeneid%5D

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ACAN%5BTI%5D%29+OR+%28aggrecan%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- AGGRECAN
  http://omim.org/entry/155760
- SPONDYLOEPIMETAPHYSEAL DYSPLASIA, AGGRECAN TYPE
  http://omim.org/entry/612813
- SPONDYLOEPIPHYSEAL DYSPLASIA, KIMBERLEY TYPE
  http://omim.org/entry/608361

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ACAN.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ACAN%5Bgene%5D
- HGNC Gene Family: C-type lectin domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/1298
- HGNC Gene Family: Hyalectan proteoglycans
  http://www.genenames.org/cgi-bin/genefamilies/set/574
- HGNC Gene Family: Sushi domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/1179
- HGNC Gene Family: V-set domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/590
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=319
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/176

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Reviewed: October 2012
Published: February 14, 2017

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